

Remarks

Claims 22-25, 32-34 and 38-46 are pending in the subject application. By this Amendment, Applicants have amended claim 22 and added new claims 47-49. Support for the amendments and new claims can be found throughout the subject specification and in the claims as originally filed (see, for example, previously presented claims 32-34, 46 and page 8, line 3 through page 9, line 30). New claims 47-49 correspond to independent claims that have been drafted to include the limitations of previously presented claims 22, 32, 33 and 34 (which appear to have been indicated as allowable in view of the comments found at page 6 of the last Office Action and the lack of any rejection made against these claims). Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 22-25, 32-34 and 38-49 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

Claims 22-25, 38, 39, 42, 43 and 44 remain rejected under 35 U.S.C. § 103(a) as obvious over Boschetti (2002) in view of Xiang *et al.* (2001) and Burton *et al.* (1998). The Office Action indicates that the teachings by Burton *et al.* provide evidence that the technique of HCIC has been successfully used to purify small proteins besides antibodies as disclosed by Boschetti. Since IL-18BP is a small protein as well as it resembles an immunoglobulin, it would be obvious for one skilled in the art to use the hydrophobic charge induction chromatography purification process as taught by Boschetti and Burton *et al.* for the purification of IL-18BP. In addition, the Office Action indicates that the reference by Xiang *et al.* discloses that IL-18BP has structural characteristics that are similar to an immunoglobulin IgG by reciting “that approximately 60% of the mature human IL-18BP resembles an immunoglobulin (IgG) domain that includes a highly conserved pair of cysteines and tryptophan residues” and by comparing it to another protein with similarities to immunoglobulin such as only about 25% amino acid sequence identity with a similar domain within the IL-1 receptor. Xiang *et al.* recites that the resemblance to IL-18BP is appropriate because IL-18 itself is not an immunoglobulin because the structural similarities of IL-18BP to an IgG disclosed by Xiang *et al.* can be utilized to purify it with methods used for the purification of immunoglobulin. Applicants respectfully assert that the claimed invention is not obvious over the cited references.

As the Patent Office is aware, all the claim limitations must be taught or suggested by the prior art in order to establish the *prima facie* obviousness of a claimed invention (*CFMT, Inc. v.*

*Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) citing *In re Royka*, 490 F.2d 981, 985 (C.C.P.A. 1974)). In this case, pyridyl matrices used in the instant application (MEP Hypercel; a resin containing 4-mercaptoethylpyridine functional groups) is loaded at pH of  $6.1 \pm 0.1$  and elution of the IL18BP is carried out at a pH of  $8.4 \pm 0.1$ . In Boschetti, the MEP column is loaded at a pH of 8.5 and the desorption of antibodies is carried out at a pH of 4.0 (see legend to Fig. 2 and the paragraph bridging pages 333-334). Burton *et al.* also teach desorption of proteins using acidic pH (see, for example, page 74, section 2.4 (teaching desorption of chymosin at a pH of 2) and page 79, section 3.5 (teaching the use of a pH of 5-5.5 for elution of proteins on various pyridyl matrices)). Thus, it is clear that the limitations of the rejected claims are not taught by the combined teachings of Boschetti and Burton *et al.* and a *prima facie* case of obviousness for the claimed invention has not been established.

Additionally, Applicants respectfully submit that modifying the teachings of Burton *et al.* and Boschetti *et al.* such that columns are loaded at an acidic pH and desorbed at a basic pH would render the methods of the prior art unsuitable for their intended purposes (namely the purification of proteins via elution using a pH gradient that becomes more acidic). Specifically (and as discussed above), both Boschetti and Burton *et al.* teach that proteins are desorbed from MEP columns by acidic pH. As noted by the Court of Appeal for the Federal Circuit, if a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. See *In re Gordon*, 733 F.2d 900, 221 U.S.P.Q. 1125 (Fed. Cir. 1984). Accordingly, reconsideration and withdrawal of the rejection of record is respectfully requested as the claimed invention is not obvious over the combined teachings of Boschetti and Burton *et al.*

It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position. Applicants expressly reserve the right to pursue the invention(s) disclosed in the subject application, including any subject matter canceled or not pursued during prosecution of the subject application, in a related application.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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